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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,663	02/08/2002	Charles Larry Bisgaier	5730-C1-01-FJT	4182

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,663	BISGAIER ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on August 12, 2003 in Paper No. 8 wherein claims 1-30 and 34-36 are cancelled (note that claims 2-9, 11-20 and 25-26 have already been cancelled in Applicant's preliminary amendment in Paper No. 6, submitted November 13, 2002), and claims 31-33 have been amended.

Currently, claims 31-33 are pending in this application.

Claims 31-33 are examined on the merits herein.

Applicant's amendment canceling claims 10, 21-24 and 27-30 and amending claims 31-33, filed August 12, 2003 in Paper No. 8 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of enablement for "the method for preventing" in claims 10, 21-24 and 27-36 of record stated in the Office Action dated February 12, 2003 has been fully considered and is found persuasive to remove the rejection since the recitation "preventing" has been removed.

Applicant's amendment canceling claims 1, 10, 21-24 and 27 filed on August 12, 2003 in Paper No. 8 with respect to the rejection of claims 1, 10, 21-24 and 27 made under 35 U.S.C. 102(b) as being anticipated by Scolnick (WO 95/06470) of record stated in the Office Action dated February 12, 2003 has been considered and found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

Applicant's amendment canceling claims 1, 10, 21-24 and 27 filed on August 12, 2003 in Paper No. 8 with respect to the rejection of claims 1, 10, 21-24 and 27 made under 35 U.S.C. 102(b) as being anticipated by JP8143454 of record stated in the Office Action dated February 12, 2003 has been considered and found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

The following is a new rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 as amended now is rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular compound of formula in claim 32-33 herein employed in a method for treating Alzheimer's disease, does not reasonably provide enablement for the employment any ACAT inhibitors to be administered for the claimed methods of the particular treatments herein in a patient.

These recitation, "an ACAT inhibitor", in claim 31, is seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention

is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method for treating Alzheimer's disease.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claim 31 is deemed very broad since the claim reads on any ACAT inhibitor employed in the claimed method of treatment herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants in claim 31, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997). The CAFC clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can

do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "an ACAT inhibitor", recited in the instant claims is purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those particular compounds of formula for the claimed method of treatment herein (see page 6 of the specification).

Thus, Applicants functional language at the points of novelty in claim 31 fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph, since it fails to provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)). The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, except

those particular compounds of formula disclosed in the specification, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the claimed method of treatment herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects for treatment of Alzheimer's disease in a human, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering any compounds represented by "an ACAT inhibitor" to a human, and/or while the patient also administering other medicines. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added).

In the instant case, in the absence of fully recognizing the identity of the members genus herein except those particular compounds of formula in the

specification, one of skill in the art would not be able to fully predict the possible treatments herein and possible adverse effects occurring with many compounds having claimed functional properties to be administered to a human in the particular claimed method herein. Thus, the teachings of the "Goodman & Gilman's" book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that the specification provides **no** working examples, i.e., testing results or data demonstrating that any ACAT inhibitors to be administered to a human, are capable of treating Alzheimer's disease in a patient.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue*

experimentation to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, for indefinite expressions the name ACAT for reasons of record stated in the Office Action dated February 12, 2003. Applicant's remarks in Paper No. 8 with respect to this rejection have been fully considered but are not deemed persuasive since Aas noted in MPEP 2111, during patent examination, claims are given their **broadest** reasonable interpretation. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim, However, it is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) for example. In the instant case, the expression "ACAT inhibitors" used to identify/describe particular compounds herein and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33 as amended now in Paper No. 8 filed on August 12, 2003 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (5,491,172, of record) in view of Scolnick (WO 95/06470, of record) for reasons of record stated in the Office Action dated February 12, 2003.

Lee et al. discloses that the instant compounds covered by the formula (I) in the patent lowers plasma-triglyceride and LDLC levels and increases HDL levels, and are useful for treating hypercholesterolemia and atherosclerosis by lowering the levels of LDL cholesterol and elevating the levels of HDL in the serum. See abstract, col.1 lines 18-60, col.2, and claims 15-16.

Lee et al. does not expressly disclose that the instant claimed compound may be useful in a method of treating Alzheimer's disease.

Scolnick discloses that statins (HMG-CoA reductase inhibitors), which are known lower plasma-triglyceride and LDLC levels and increase HDL levels, are useful in methods of treating Alzheimer's disease. Moreover, Scolnick teaches that the reduction of cholesterol and plasma-triglyceride and LDLC levels may decrease risk of

development of Alzheimer's disease and treat vascular related diseases such as Alzheimer's disease. See abstract, page 2 lines 16-20, page 10, and claims 1-25.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the instant compounds in methods of treating the onset of Alzheimer's disease herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the instant claimed compounds in methods of treating Alzheimer's disease since the instant compounds are known to be useful for lowering plasma-triglyceride and LDLC levels and treating hypercholesterolemia. It is also known that the reduction of plasma-triglyceride and LDLC levels may decrease risk of development of Alzheimer's disease and treat vascular related diseases such as Alzheimer's disease. Therefore, one of ordinary skill in the art would have reasonably expected that the instant compound would have beneficial therapeutic effects and usefulness in the method of treating Alzheimer's disease by reducing or lowering plasma-triglyceride and LDLC levels in patients suffering therefrom.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on August 12, 2003 in Paper No. 8 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Applicants assert that there is nothing in the cited prior art providing the motivation to substitute ACAT inhibitors in treating Alzheimer's disease taught in Scolnick since the mechanism of action of ACAT inhibitors herein differs from the prior art. However, as discussed in the rejection under 35 U.S.C. 112, first paragraph, set forth above, the specification provides **no** working examples, i.e., testing results or data demonstrating that any ACAT inhibitors to be administered to a human, are capable of treating Alzheimer's disease in a patient. Therefore, there is no clear and convincing evidence of nonobviousness or unexpected results in specification herein in support the nonobviousness of the instant claimed invention over the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
October 22, 2003